REMARKS

Claim Rejections Under 35 USC § 103

The Office Action rejects claims 1-6, 9, 11-13 and 23 as allegedly obvious by different combinations of Petrigni (US 2004/0136925 A1), Sakurai (US 4,716,224), Wilkinson (*"The Pharmacological Basis of Therapeutics"*, McGraw-Hill, 2001, 24-26), Sterling (British Journal of Dermatology (2001), 144, 4-11), Falk (US 5,914,322) and Fischer (US 6,455,066), as set forth below.

(a) Combination of Petrigni and Sakurai

Under item 1, the Office Action alleges that claims 1-4, 6, 9 and 11-13 are obvious by a combination of Petrigni and Sakurai.

Petrigni discloses a pharmaceutical composition for treating pathological skin diseases, which composition comprises, as active ingredient, a mixture of hyaluronic acids of various molecular weight (200 kDa to 4000 kDa). According to the citation, specific examples of such skin diseases comprise acne vulgaris, psoriasis and atopical eczema (cf. page 1, paragraphs [0001], [0010], [0012] and [0013]).

Sakurai discloses hyaluronic acid in crosslinked form having a crosslinking degree of between 0.75% to 4% as well as its use for a cosmetic treatment of the skin. According to the citation, hyaluronic acid in crosslinked form has the advantage that it is resistant to enzymatic and oxidative/reductive degradation while maintaining different properties of uncrosslinked hyaluronic acid.

According to the Office Action's view, claim 1 of the present application differs from Petrigni in that it makes use of crosslinked hyaluronic acid instead of uncrosslinked hyaluronic acid. Allegedly, the substitution of uncrosslinked to crosslinked hyaluronic acid is obvious because the use and the advantages of crosslinked hyaluronic acid was already known from Sakurai.

However, one of ordinary skill in the art aiming to provide a method for treating inflammatory skin or mucous membrane diseases would not consider intradermally administering crosslinked hyaluronic acid due to the latter having completely different properties as compared to uncrosslinked hyaluronic acid.

Going into details, crosslinked hyaluronic acid, due to crosslinking and its high molecular weight, has a high viscosity and, thus, is a jelly-like compound which behaves like a solid and is therefore degraded in living organisms by phagocytosis. Moreover, due to its physicochemical properties, crosslinked hyaluronic acid does not laminarily distribute within the tissue following

intradermal administration, but accumulates in the form of clusters. Hence, in contrast to uncrosslinked hyaluronic acid, the principles of pharmacology and pharmacokinetics do not apply for crosslinked hyaluronic acid.

In consequence, a person skilled in the art would not consider combining the teachings of Petrigni and Sakurai since crosslinked hyaluronic acid was not believed to be suitable for treating inflammatory skin diseases by administering the compound intradermally at the time the invention was made.

A declaration in support of the above will be filed in the near future.

(b) Combination of Petrigni, Sakurai and Wilkinson

Under item 2, the Office Action alleges that claim 5 is obvious by a combination of Petrigni, Sakurai and Wilkinson.

Wilkinson is concerned with the pharmacokinetics of drug absorption, distribution and elimination. According to the citation, the intensity of a drug's effect is related to its concentration above a minimum effective concentration, whereas the duration of this effect is a reflection of the length of time the drug level is above this value. In order to use a drug's therapeutic window, the drug is generally administered in a series of repetitive doses or as a continuous infusion to maintain a steady-state concentration of drug above the minimum effective concentration (cf. pages 24-26).

Allegedly, one of ordinary skill in the art was aware of uncrosslinked hyaluronic acid taking effect faster than crosslinked hyaluronic acid. Thus, in order to increase the therapeutic window of hyaluronic acid, the skilled person was allegedly motivated to administer a mixture of crosslinked and uncrosslinked hyaluronic acid for treating inflammatory skin diseases.

The objection is unjustified and is based on an inadmissible hindsight analysis. As regards claim 1, the Office Action alleges that one of ordinary skill in the art would replace the uncrosslinked hyaluronic acid of Petrigni by the crosslinked hyaluronic acid of Sakurai due to crosslinked hyaluronic acid providing distinct advantages over uncrosslinked hyaluronic acid. Turning to claim 5, on the other hand, the Office Action alleges that one of ordinary skill in the art would nevertheless use uncrosslinked hyaluronic acid in addition to crosslinked hyaluronic acid although uncrosslinked hyaluronic acid is allegedly unfavourable. Thus, the Office Action's argumentation is inconsistent, and in any event goes beyond what one of ordinary skill in the art would understand from the disclosures of the cited references.

Moreover, Wilkinson only generally relates to drug absorption, distribution and elimination, and does not mention hyaluronic acid at all. The Office Action has not provided any

kind of evidence in support of the allegation that uncrosslinked hyaluronic acid actually takes effect faster in the organism than crosslinked hyaluronic acid. This allegation is rather speculative and is unsupported.

In particular, one of ordinary skill in the art would not rely on Wilkinson when employing crosslinked hyaluronic acid for the treatment of inflammatory skin diseases due to the principles of pharmacology and pharmacokinetics not being applicable to crosslinked hyaluronic acid for the reasons set out under item (a). Consequently, due to the skilled person not being motivated to combine the teachings of Petrigni, Sakurai and Wilkinson, one cannot arrive at the subject-matter of claim 5 based on this combination of documents.

(c) Combination of Petrigni, Sakurai and Sterling

Under item 3, the Office Action alleges that claim 23 is obvious by a combination of Petrigni, Sakurai and Sterling.

Sterling is concerned with guidelines for the management of cutaneous warts and discloses that warts are caused by infection of the epidermis with human papilloma virus (cf. page 4, left column). The Office Action alleges that it was thus obvious to employ Petrigni's composition for treating viral skin diseases which lead to wart formation.

The rejection is unjustified. As set out under item (a) above, Petrigni discloses a composition for treating pathological skin diseases by means of hyaluronic acid. However, the citation is completely silent regarding the treatment of skin diseases caused by viral infections.

As pointed out in the response to the Office Action dated 24 October 2008, inflammations of the skin can be caused by many different factors. Atopic dermatitis (cf. Example 1 of the application) is a disease primarily aggravated by contact with or intake of allergens. Acne vulgaris (cf. Example 3) is a result of changes in the pilosebaceous units of the skin, whereas viral warts (cf. Example 2) are caused by a viral infection. Consequently, the skilled person would not expect Petrigni's composition to be also suitable for treating viral skin diseases.

(d) Combination of Falk, Sakurai and Fischer

Under item 4, the Office Action alleges that claims 1-4, 9, 11-13 and 23 are obvious by a combination of Falk, Sakurai and Fischer.

Contrary to the Office Action's allegation, Fischer does not teach intradermal administration of penetration agents for improving the absorption of a drug. Whereas Fischer mentions the possibility as well as the advantages of intradermal administration as compared to topical application, the citation does not propose intradermal administration of drugs which are hard to administer via the topical route, but topical administration of the drug by applying the

same in combination with a suitable penetration agent.

Thus, in case intradermal application of a drug is intended, no penetration agent is needed. Consequently, a person skilled in the art combining the teachings of Falk and Fischer would arrive at a composition wherein either an inhibitor of prostaglandin synthesis is topically applied together with hyaluronic acid as the penetration agent, or an inhibitor of prostaglandin synthesis is intradermally administered in the absence of hyaluronic acid.

Irrespective of that, a person skilled in the art would not consider combining the teachings of Falk and Sakurai for at least the reasons set out under item (a) above.

(e) Combination of Falk, Sakurai, Fischer and Wilkinson

Under item 5, the Office Action alleges claims 5 and 6 are obvious by a combination of Falk, Sakurai, Fischer and Wilkinson.

The objection is unjustified for the reasons set out herein before under items (a), (b) and (d) and should be withdrawn.

Reconsideration is respectfully and courteously requested.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,

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